Notice of Allowability	Application No.	Applicant(s)	
	09/687,855	KHOSLA ET AL.	
	Examiner	Art Unit	
	Kathleen M. Kerr	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *12/30/04*.

2. ☒ The allowed claim(s) is/are *61,63-69,71-74 and 78-92*.

3. ☐ The drawings filed on _____ are accepted by the Examiner.

4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.
THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

5. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

6. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
   (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

   Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).

7. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. ☐ Notice of References Cited (PTO-892)
2. ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3. ☐ Information Disclosure Statements (PTO-1449 or PTO/SB/08), Paper No./Mail Date _____
4. ☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
5. ☐ Notice of Informal Patent Application (PTO-152)
6. ☐ Interview Summary (PTO-413), Paper No./Mail Date _____ .
7. ☒ Examiner's Amendment/Comment
8. ☐ Examiner's Statement of Reasons for Allowance
9. ☐ Other _____.

Kathleen M Kerr
Primary Examiner
Art Unit: 1652

DETAILED ACTION

Application Status

1. In response to the previous Office action, a non-final rejection (mailed on September 27, 2004), Applicants filed a response and amendment received on December 30, 2004. Said amendment cancelled Claims 1, 55-56, 58-60, and 75-77, amended Claims 69, 79, and 82, and added new Claims 84-85. Thus, Claims 61, 63-69, 71-74, 78-85 are pending in the instant Office action.

Priority

2. As previously noted, the instant application is granted the benefit of priority for the U.S. Provisional Application Nos. 60/159,090 filed on October 13, 1999, 60/206,082 filed on May 18, 2000 and 60/232,379 filed on September 14, 2000.

Withdrawn - Objections to the Specification

3. Previous objection to the specification because the title is not descriptive is withdrawn by virtue of Applicant's amendment to the title.

Withdrawn - Claim Rejections - 35 U.S.C. § 112

4. Previous rejection of Claims 79 and 82 under 35 U.S.C. § 112, second paragraph, as being indefinite is withdrawn by virtue of Applicant's amendment.

EXAMINER'S AMENDMENT

5. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 C.F.R. § 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment to the claims was given in a telephone interview with Carolyn Favorito on March 14, 2005.

Amendments to the Specification

6. The specification has been amended as follows:

a) Delete the Abstract and replace with the following Abstract:

---The use of enzymes that catalyze the production of starter and extender units for polyketides in *E. coli* and *Streptomyces* is described; these enzymes include malonyl CoA decarboxylase (MatA), malonyl CoA synthetase (MatB), and a malonate transporter (MatC) as well as proprionyl CoA carboxylase (pcc). The *mat*BC gene from *Streptomyces coelicolor*, the *mat*ABC genes from *Rhizobium trifoli*, and the *pcc*B and *acc*A2 from *Streptomyces coelicolor* are useful in specific embodiments of the claimed invention. These enzymes may be used to enhance the yield of polyketides that are natively produced or polyketides that are rationally designed. By using these techniques, the synthesis of a complete polyketide has been achieved in *E. coli* in the presence of a phosphopantetheinyl transferase, such as *sfp* from *Bacillus subtilis*. This achievement permits a host organism with desirable characteristics to be used in the production of such polyketides and to assess the results of gene shuffling.---

Amendments to the Claims

7. The claims have been amended as follows:

a) Rewrite Claim 68 as follows:

---68. The host cell as in claim 61

wherein the polyketide is 6-dEB.---

b) Rewrite Claim 69 as follows:

---69. A recombinant *E. coli* host cell which is genetically modified for synthesis of a polyketide, wherein said modification comprises:

a) incorporation of the *mat*BC gene from *Streptomyces coelicolor* or the *mat*BC gene from *Rhizobium trifoli*,

b) incorporation of at least one expression system for a modular polyketide synthase, and

c) incorporation of the *sfp* gene from *Bacillus subtilis*.---

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c) Rewrite Claim 79 as follows:

---79. A method to assess polyketide production in a host cell containing shuffled polyketide synthase (PKS) genes, said method comprising:

a) shuffling PKS genes or functional domains thereof to produce a mixture of rearranged PKS genes,

b) transforming a culture of *Streptomyces* according to Claim 61 with said mixture,

c) culturing individual colonies of said transformed *Streptomyces*, and

d) assessing each colony for polyketide production,

wherein colonies, which produce polyketides, contain successfully shuffled genes.---

d) Rewrite Claim 82 as follows:

---82. A method to assess polyketide production in a host cell containing shuffled polyketide synthase (PKS) genes, said method comprising:

a) shuffling PKS genes or functional domains thereof to produce a mixture of rearranged PKS genes,

b) transforming a culture of *E. coli* according to Claim 69 with said mixture,

c) culturing individual colonies of said transformed *E. coli*, and

d) assessing each colony for polyketide production,

wherein colonies, which produce polyketides, contain successfully shuffled genes.---

e) Rewrite Claim 84 as follows:

---84. A recombinant *E. coli* host cell which is genetically modified for synthesis of a polyketide, wherein said modification comprises

a) incorporation of a propionyl CoA carboxylase (pcc) expression system comprising the *pcc*B and *acc*A2 genes from *Streptomyces coelicolor* wherein said pcc expression system produces an enzyme capable of synthesizing 2S-methylmalonyl CoA,

b) incorporation of at least one expression system for a modular polyketide synthase, and

c) incorporation of the *sfp* gene from *Bacillus subtilis*;

wherein the cell's prpA-D operon is deleted.---

f) Add new Claims 86-92:

---86. A method to assess polyketide production in a host cell containing mutated polyketide synthase (PKS) genes, said method comprising:

a) mutating PKS genes to produce a mixture of mutated PKS genes,

b) transforming a culture of *Streptomyces* according to Claim 61 with said mixture,

c) culturing individual colonies of said transformed *Streptomyces*, and

d) assessing each colony for polyketide production,

wherein colonies, which produce polyketides, contain successfully mutated genes.

87. A method to assess polyketide production in a host cell containing mutated polyketide synthase (PKS) genes, said method comprising:

a) mutating PKS genes to produce a mixture of mutated PKS genes,

b) transforming a culture of *E. coli* according to Claim 69 with said mixture,

c) culturing individual colonies of said transformed *E. coli*, and

d) assessing each colony for polyketide production,

wherein colonies, which produce polyketides, contain successfully mutated genes.

88. A method to assess polyketide production in a host cell containing shuffled polyketide synthase (PKS) genes, said method comprising:

a) shuffling PKS genes or functional domains thereof to produce a mixture of rearranged PKS genes,

b) transforming a culture of *E. coli* according to Claim 84 with said mixture,

c) culturing individual colonies of said transformed *E. coli*, and

d) assessing each colony for polyketide production,

wherein colonies, which produce polyketides, contain successfully shuffled genes.

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89. A method to assess polyketide production in a host cell containing mutated polyketide synthase (PKS) genes, said method comprising:

a) mutating PKS genes to produce a mixture of mutated PKS genes,

b) transforming a culture of *E. coli* according to Claim 84 with said mixture,

c) culturing individual colonies of said transformed *E. coli*, and

d) assessing each colony for polyketide production,

wherein colonies, which produce polyketides, contain successfully mutated genes.

90. The method of claim 85, which further includes providing a substrate, wherein the substrate is of the formula $RCH(COOH)_2$ wherein R is H, methyl or ethyl.

91. The methods of claim 79, wherein said host cell is *Streptomyces coelicolor.*

92. The method of claim 86, wherein said host cell is *Streptomyces coelicolor.*---

Conclusion

8. Claims 61, 63-69, 71-74, and 78-92 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M. Kerr whose telephone number is (571) 272-0931. The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kathleen M Kerr
Primary Examiner
Art Unit 1652

March 14, 2005